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10/588,235	08/03/2006	Robert William Ward	0020-5499PUS1	5422

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EXAMINER	
RAO, SAVITHA M	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
03/19/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/588,235	WARD ET AL.	
	Examiner	Art Unit	
	SAVITHA RAO	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *17-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/18/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-20 are pending.

Claims 17-19 are withdrawn from consideration as being drawn towards a nonelected invention.

Claims 1-16 and 20 are under consideration in the instant office action.

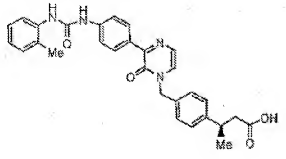
Election/Restrictions

Applicant's election with traverse of Group I (claims 1-12, 13-15,16 and 20) in the reply filed on 01/12/2009 is acknowledged. The traversal is on the ground(s) that their exists no undue search to search and consider all claims in their entirety and that the claims are linked so as to form a single general inventive concept burden exists to examine the claims in a single application.

Examiner finds the applicant's argument unpersuasive and maintains the restriction since as the Groups are patentably distinct and independent since they lack unity as set forth in the restriction requirement dated 12/12/2008 (pages 4-6). The subject matter clearly lacks unity of invention for the reasons given in the restriction requirement and, thus, the claims are directed to patentably distinct inventions and, because of the distinct nature of the inventions, do not constitute overlapping subject matter that would result in a coextensive search.

Additionally, it is noted that Applicant's have failed to address the non-statutory status of instant claim 16 as noted in the beginning of the restriction requirement dated 12/12/2008 (page 2).

Applicant's election of the following compound as a single specie of compound for examination is acknowledged



Claims under consideration in the current office action are claims 1-16 and 20 which read on the elected subject matter of Group I.

However, upon further reconsideration examiner withdraws the election of specie requirement.

Claims 17-19 are withdrawn as being drawn to non-elected invention.

Applicant timely traversed the restriction (election) requirement in the reply filed on 01/12/2009

Restriction for examination purposes as indicated is proper and is therefore made FINAL.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 16 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 provides for the use of the elected compound of formula (I) in the manufacture of a medicament for the treatment or prevention of conditions in which an inhibitor of alpha-4 integrin mediated cell adhesion is beneficial., but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

For the purposes of the instant office action claim 16 is being interpreted as being drawn to a composition comprising the compound of formula (I) .

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement:

Claims 1-16 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention as claimed. While the applicant clearly provides method of preparation of the instantly elected compound, applicants fail to provide adequate support in the disclosure to demonstrate the mechanism of action of the instantly claimed compound and data demonstrating the use of the instantly elected compound.

As stated in the MPEP 2164.01(a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

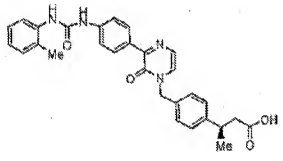
In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). These factors include, but are not limited to:

(A) The breadth of the claims;
(B) The nature of the invention;

(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

All of these factors have been considered with the most relevant ones discusses below.

The nature of the invention and the breadth of the claims. The nature of the invention is the following product, its method of preparation and pharmaceutical composition comprising the elected compound (shown below) or its pharmaceutically acceptable derivative thereof.



The invention is complex in that these are novel compositions of matter. The breadth of the claims exacerbates the complexity of the invention. The instant breadth of the rejected claims is broad and the recitation of "pharmaceutical derivatives of the elected compounds" renders the claim very broad as it includes several structurally distinct compounds with a common core structure of the elected compound.

The amount of direction or guidance present and the presence or absence of working examples. With respect to making the instant compound: The instant

specification provides ample guidance for making the compound claimed in the instant claims as shown in Examples 1 (pages 43 of the instant disclosure) . There is no data present in the specification for the preparation of derivatives of the compound of example 1. The specification merely states "...or a pharmaceutically acceptable derivative thereof ". Additionally, preferred embodiments and examples do not support enablement for derivatives of the elected compound.

With respect to the mechanism of action of the instant compound or using the instant compound: The instant specification and claims allege that the compound have use as $\alpha 4$ integrin inhibitors. However, no data is provided in the instant disclosure demonstrating the utility of the instantly claimed compound as integrin inhibitors. Although applicants, recite the Jurkat J6 Scintillation proximity Assay (SPA) method as a possible method which may be used to test the compounds activity against integrin VLA-4 expressed Jurkat J8 cells, other than giving a blanket statement that all the tested compounds possessed pKi $\leq$ 8.0 does not provide actual data of the study with specific compounds tested, nor does the specification disclose the mechanism of action of the instantly claimed compounds in terms of the alleged inhibition of integrin receptors.

The exact PKi obtained with the instant compound is not shown and the comparison of the performance of the instant compound with the standard is not disclosed. Also, it is not clear as to the significance of the Pki obtained in relation to the actual use of these compounds. Only reference to the mechanism of the instant compound is on page 15 of the instant disclosure where Applicant recites that the

compounds of formula (I) inhibit $\alpha 4$ integrin mediated cell adhesion. However, no support is provided as to how the specifically claimed compound acts to inhibit the $\alpha 4$ integrin cell adhesion.

Instant claim 13 recites the intended use for therapy of the instant compound. However, applicant fails to provide what the intended therapy is. It is unclear what "therapy" is intended in the instant claim.

The quantity of experimentation needed. While the level of skill in the pharmaceutical arts is high, it would require undue experimentation for one of ordinary skill in the pertinent art to test the instantly claimed compound for selective VLA-4 inhibitory activity. Although applicants have clearly demonstrate methods of preparing the instantly claimed compound, absence of any data suggesting the mechanism of action and use of these compounds as anti-integrin agents puts undue burden on the ordinarily skilled artisan to use the compound as claimed.

Genetech Inc. V. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors discussed above, to use the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to determine which, if the instant compound exhibit VLA-4 inhibition.

Thus, rejection of claims 1-16, 20 under 35 U.S.C. §112, first paragraph, is deemed proper.

Written description:

Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a Written Description rejection.

Regarding the requirement for adequate written description of chemical entities, Applicant's attention is directed to the MPEP §2163. In particular, *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089, 118 S. Ct. 1548 (1998), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plain for obtaining the claimed chemical invention." *Eli Lilly*, 119 F.3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications under the 35 U.S.C. 112.I "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia*, "functional characteristics when coupled with a known or disclosed correlation between function

and structure..." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 316, 1324-25 (Fed. Cir. 2002) (quoting *Guidelines*, 66 Fed. Reg. at 1106 (emphasis added)). Moreover, although *Eli Lilly* and *Enzo* were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in general. *Univ. of Rochester v. G.D. Searle & Co.*, 249 Supp. 2d 216, 225 (W.D.N.Y. 2003).

In the instant case, Claims 1, 2, 6, 7, 11 and 12 recites a genus of "derivatives". There is insufficient evidence for derivatives as claimed in the instant disclosure. Regarding the term " a pharmaceutically acceptable derivative thereof" of the elected compound, due to the great number and variety of compounds included in the scope of "derivatives" applicants are not found to be in possession of a representative number of species that sufficiently represent the great variety of such compounds, which is required to claim all 'derivatives there of instantly elected compounds. It is noted that applicants provide an list of compounds E1 to E18 on pages 43-48 of the specification, E1 being the instantly elected compound. It is not clear from the disclosure if the compound E2 to E8 are indeed the derivatives of E1. Even if they are, they only represent a subset of the number of compounds encompassed by the term "derivatives". Giving the term 'derivatives thereof its broadest reasonable interpretation, the number and types of compounds which can be considered derivatives of formula (I) is exponentially greater, and can be interpreted to include elemental carbon, nitrogen and hydrogen as 'derivatives of compound of formula (I).' Applicants have not specifically defined what characteristics of the compound the claimed "derivatives" must

have; applicants have not identified any particular core chemical structure or function which must be shared by all derivatives thereof; and thus one of ordinary skill in the art would not immediately envisage all derivatives of the compound of formula (I).

.Accordingly, for an ordinarily skilled artisan to test every derivative of the claimed compounds would impose undue burden. The need for testing amongst varying species of compounds to determine the full scope of the genus of derivatives as instantly claimed demonstrates that applicants were not in possession of the full scope of the genus now presently claimed. "Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the Applicant was in possession of the claimed invention." Please see MPEP § 2163. Applicants are imposing the burden of extensive testing upon the skilled artisan to identify those other agents that may have any of the disclosed functions, but which Applicants have not identified and thus, were not in possession of, at the time of the present invention. It has been held in patent law that a wish or plan for obtaining the invention as claimed does not provide adequate written description of a chemical invention. Rather, a precise definition, such as by structure, formula, chemical name or physical properties or a combination thereof, is required. Please reference, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004). In other words, though Applicants may have a plan for how to identify other derivatives of the instantly claimed compound

that may be amenable for use in the present invention, it remains that at the time of the invention Applicants had not identified such compounds, and, therefore, did not have written description of the full scope of the genus claimed.

Conclusion

Claims 1-16 and 20 are rejected. No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAVITHA RAO whose telephone number is (571)270-5315. The examiner can normally be reached on Mon-Fri 7 am to 4 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached at 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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